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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/756,125	01/12/2004	Dennis R. Burton	48503-00004	3579

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 06/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/756,125	BURTON ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,9-17,19-22,28-36,38-41,47-55,57-60,66-74,76-79,85-93 and 95* is/are pending in the application.

4a) Of the above claim(s) *11-14,30-33,49-52,68-71 and 87-90* is/are withdrawn from consideration.

5)☒ Claim(s) *1-3,9,15-17,19-22,28,29,34-36,38-41,47,53-55,57-60,66 and 72-74* is/are ~~allowed~~. allowable. SPE 6/9/06

6)☒ Claim(s) *10,48,67,76-79,85,86,91-93 and 95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed March 31,2006 is acknowledged and entered. Claims 1-3, 9, 10, 15-17, 19-22, 28, 29, 34-36, 38-41, 47, 48, 53-55, 57-60, 66, 67, 72-74, 76-79, 85, 86, 91-93 and 95 are under examination. Claims 11-14, 30-33, 49-52, 68-71 and 87-90 remain withdrawn from consideration, being drawn to non-elected inventions.

2. The following objections and rejections are withdrawn:

- The objection to the specification for containing embedded hyperlinks is withdrawn in view of Applicant's amendment to the specification removing the hyperlinks.
- The objections to claims 1-3, 9, 10, 15-17, 19-22, 28, 29, 34-36, 38-41, 47, 48, 53-55, 57-60, 66, 67, 72-74, 76-79, 91-93 and 95 for reciting non-elected subject matter, is withdrawn in view of Applicant's amendment to the claims removing the non-elected subject matter.
- The rejection of claims 1-3, 10, 15, 19-22, 29, 34, 38-41, 47-48, 57-60, 66-67, 72-74, 76-79, 85, 86, 91-93 and 95 is withdrawn with respect to claims 1-3, 10, 15, 19-22, 29, 34, 38-41, 47-48, 57-60, 66-67, 72-74, 76, 85, 86 and 95, in view of Applicant's amendments and persuasive arguments.

Claim Rejections - 35 USC § 112

3. Claims 77-79 and 91-93 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 77-79 and 91-93 are drawn to antibodies. Claim 77 recites, "An isolated population of monoclonal mammalian anti-Dengue virus antibodies, comprising at least one human CDR, wherein said antibodies specifically bind at least one epitope comprising at least 1-3 amino acids, to the entire amino acid sequence of a Dengue virus NS protein." It is unclear what is meant by "to the entire amino acid sequence of a Dengue virus NS protein". Does Applicant intend to claim antibodies that bind anywhere along the NS protein? Does Applicant mean that there is a single epitope that is comprised of the entire amino acid sequence of the NS protein? Does Applicant mean that the antibodies bind multiple epitopes along the NS protein? The metes and bounds of the claims cannot be determined without further definition. The meaning of the claim cannot be discerned. Correction and clarification are required to overcome this rejection.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(*New Rejection*) Claims 10, 48, 67 and 86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to compositions comprising antibodies to Dengue NS1, and a therapeutically or prophylactically effective amount of at least one compound or protein selected from the group consisting of a detectable label or reporter, a Dengue virus replication antagonist, a non-steroid anti-inflammatory drug (NSAID), an analgesic, an anesthetic, a sedative, a local anesthetic, and antimicrobial, a corticosteroid, an erythropoietin, an antigen for immunization, an immunoglobulin, a growth hormone, a hormone replacement drug, a radiopharmaceutical, an asthma medication, an inhaled steroid, an epinephrine or analog, a cytokine, and a cytokine antagonist. *The claims encompass a large genus of molecules that are therapeutic or prophylactic, for which Applicant has not adequately demonstrated possession.*

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

In this case, the claimed composition comprises an anti-Dengue NS1 antibody and a molecule that imparts a therapeutic benefit, or a preventative benefit (prophylactic). While the claims do not mention exactly what is to be treated or prevented, the composition as a whole encompasses molecules that are not known to be therapeutic or prophylactic against Dengue virus, or any other pathogen.

For example, a therapeutic or prophylactic composition comprising anti-Dengue NS1 antibody in addition to an amount of any cytokine: What condition is the cytokine going to prevent? And, given the condition, what type of structural features and functions should the particular cytokine possess? In the case of a detectable label or reporter: What condition is that molecule going to treat or prevent, and what properties should the label have? These same questions apply to all of the molecules listed in the claims. Without a structure/function nexus, one of skill in the art would not be put in possession of the large genus of molecules encompassed by the claims.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required.

See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived.

Claim Rejections - 35 USC § 102

5. Claims 76-79, 85-86, 91-93 and 95 are rejected under 35 U.S.C. 102(b) as being anticipated by Valdés *et al.* (*Clinical and Diagnostic Laboratory Immunology*, 2000, 7(5):856-857, "Valdés"). Previously, claim 76 was not rejected, however, the amendment to the claim necessitates its rejection.

The claims are drawn to isolated antibodies, populations of antibodies, compositions, medical devices and articles of manufacture for pharmaceutical or diagnostic use. The antibodies specifically bind at least one epitope comprising at least 1-3 amino acids of the Dengue NS protein, specifically the NS1 protein. Specifically, the antibodies bind to the same region of a Dengue virus protein as an antibody comprising at least one light chain CDR having the amino acid sequence of SEQ ID NO: 4. The compositions further comprise other compounds or proteins, such as labels, NSAIDS, sedatives, antimicrobials, immunoglobulins and others. The medical devices are comprised of the antibodies and are suitable for a variety of modes of delivery. The article of manufacture for human pharmaceutical or diagnostic use comprises the antibodies, packaging material and a container. The antibody has a human CDR. Claim 95 is drawn to an anti-Dengue virus antibody produced by a method according to cancelled claim 94. While this claim is indefinite, the broadest interpretation of the claim has been used, and thus claim 95 is included in this rejection for purposes of compact prosecution.

Valdés discloses human Dengue antibodies against structural and nonstructural proteins, including antibodies against NS1 (abstract). The antibodies were isolated from patients infected with Dengue virus. These antibodies are human and therefore contain human CDRs. It is entirely expected that the antibodies against NS1 bind an epitope that is at least 1-3 amino acids in length, if not longer. With regard to the antibody binding the same region of a Dengue virus as the antibody comprising SEQ ID NO: 4, the region bound by the latter antibody is NS1. Valdés' antibody binds NS1. If Applicant is referring to the exact epitope where the paratope SEQ ID NO: 4 binds, then Applicant is required to show that epitope. Lacking further specifics on where the antibody binds, the "regions" is considered to be NS1, and thus Valdés' antibodies meet the claim limitations. With regard to the limitation that the composition comprises at least a pharmaceutically acceptable carrier or diluent (claim 85), the serum samples taken from the patients were diluted during the Western blot analysis of the antibodies (page 856, second column, first paragraph). The antibody solution that is prepared for Western blot contains more than one antibody (immunoglobulin), a population, thus reading on the claims. With regard to the therapeutic or prophylactic amount, the claims do not specify what is to be treated or prevented. Lacking any intention, the antibodies contained in the solution qualify as additional therapeutic proteins.

Applicant's arguments have been carefully considered but fail to persuade. Applicant argues that Valdés does not disclose a medical device or a delivery device or system which uses one of the modes recited in claim 93 comprising the anti-Dengue virus antibody. Particularly, Applicant argues that classical Western blots are performed by loading protein antigens into an electrophoresis gel and antibodies are used as probes in solution. Therefore, the antibodies of

Valdés were not present in a medical device suitable for administration via the modes in claim 93.

In response to Applicant's argument, the examiner has reviewed the excerpt (Applicant's attachment) regarding Western blotting. As Applicant points out, the protein antigens are loaded into the gel, in this case, Dengue antigens. In the method of Western blotting, the anti-Dengue antibodies were not loaded into the gel.

However, note that antibodies to NS1 were detected in 40% of patients (secondary infections), page 856, column 1, third paragraph. Serum samples from the patients were taken, presumably by needle. The syringe containing the serum samples from the patients having antibodies to anti-Dengue NS1, reads on the claimed invention. The syringe is useful for diagnostic uses and medical devices in non-human animals, and even humans, and can be administered in a variety of ways, such as those listed in claim 91. The syringe itself is a container and packaging material (plastic or glass tube with the syringe and a plastic plunger). Given the broadest reasonable interpretation of the claims, Valdés anticipates the claimed invention.

Conclusion

6. Claims 10, 48, 67, 76-79, 85-86, 91-93 and 95 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Stacy B. Chen 6/8/06

Stacy B. Chen
Primary Examiner
June 8, 2006